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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/184,572	11/02/1998	LISA MCKERRACHER	99999/MARUSY	4396

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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/184,572	MCKERRACHER ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-29,43 and 45-47* is/are pending in the application.

4a) Of the above claim(s) *25-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43 and 45-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *25-29,43 and 45-47* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3-11-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5,10-0

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3-11-05 has been entered.

2. The amendment filed 3-11-05 has been entered into the record and has been fully considered.

3. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

4. As a result of Applicant's amendment, all rejections not reiterated herein are withdrawn.

5. Claims 25-29, 43 and 45-47 are pending.

6. Claims 25-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Specification

7. The disclosure is objected to because of the following informalities: Applicant's referral to an apparent error in citation of a noted reference pertaining to p. 3, lines 11-13 is recognized as pointed out within the 3-11-05 response, see in particular p. 6-7

paragraph spanning. No correction is noted within the specification. The Examiner is also unclear as to the correctnesss of the new citation in that the Lamourexux reference is not notably directed to L1 experimentation with astrocytes.

Consideration and any appropriate correction is requested.

Priority

8. Reconsideration of the priority determination with respect to the newly amended claims and Applicants arguments is considered persuasive to provide benefit to the 10-31-97 date as supported within the 2,214,841 application.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-2, 6-13, 17 and 21-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamata et al., Microbiol., Immunol., 38(6):421-428, 1994, Johnson et al., US Patent No. 5,851,786 issued 12-22-98, filed 9-27-95, Varon et al., J. of Neurotrauma 11(5):473-486, 1994, Mobley et al., 5,134,121 July 28, 1992, Mattson et al., Stroke 1993, 24(12):I136-40; discussion I144-5, Olson et al., J. of Neurol., 1994 Dec., 242 (1Suppl. 1):S12-15 and Olson et al., Acta Neurochirurgica Supplementum, 1993, 58(3-7).

Kamata et al., teach chick dorsal root ganglia (DRG) induced nerve outgrowth via administration of C botulinum C3 exoenzyme (ADP-ribosyltransferase) that is at least as

effective as DRG outgrowth induced via the neurotropic factor NGF, a noted neurotrophic factor recognized as being effective in in vitro and in vivo use for stimulating neurite outgrowth both within CNS and PNS and within neuronal or spinal cord injury including following surgery, see in particular abstract, Effects of C3 exoenzyme on the morphology of cultured cells, pp. 424-425 pp. 427, lines 2-23. Based on such evidence Kamata et al., conclude that C3 exoenzyme is a neurotropic agent. DRG cells contain both central and peripheral projections and thus the outgrowth is of CNS although the outgrowth is in culture.

Johnson et al., teach a method of treating an individual to regulate actin polymerization, stress fiber formation and/or focal adhesion assembly by administration of a compound such as Botulinum C3 exoenzyme also known as ADP-ribosyl C3 transferase at 100ng/ul, see in particular column 14, line 56-line 15, line 59, column 18, lines 30-63 and Example 3, including administration directly to a cell in vivo, ex vivo or systemically, see in particular column 18, line 44. Additionally administration is as in column 15-16 including subcutaneous, intramuscular or transdermal. The administration may be measured functionally including detecting neuronal response and for a therapeutic composition for the treatment of Parkinson's or Alzheimer's disease, see in particular Abstract and column 17, lines 18-58 and claim 40. As the administration routes are systemic the administration necessarily results in the administration at sites of lesion including to neurons within the PNS and CNS. It is further noted that the method is effective to treat Alzheimer's and Parkinson's disease which are recognized as affecting CNS brains neuronal cells which exhibit focal lesions.

Kamata et al., et al., teaches that C3 ADP-ribosyl transferase acts as a neurotrophic factor to PNS and CNS cells (DRG ganglia) in vitro, similar to nerve growth factor. Johnson et al., teaches administration of C3 ADP-ribosyl transferase to patients for treatment of neurological disorders with notable effects being equated to regeneration or the re-establishment of functional connections and repair of damaged neuronal cell pathways.

Kamata et al., and Johnson et al., and fail to teach in vivo administration of C3 exoenzyme via infusion into a site of surgery for spinal cord lesion to increase neurite regeneration in spinal cord lesion following damage and to promote regeneration and neuronal outgrowth within the CNS in a patient.

Varon et al., teach that neurotrophic factors are well recognized for their important function on developing neurons of the PNS, to prevent or reduce degenerative responses of adult CNS to a variety of diseases and injuries, and in the regeneration of adult CNS in animals. Varon et al., further teach various model systems utilizing in vivo administration of NGF to promote neuronal outgrowth in the CNS in vivo. NGF is a molecule that has been isolated as a neurotophic factor based upon it's ability to promote neurite outgrowth in dorsal root ganglia assays including following surgery or operation.

Mobley et al., similarly teach NGF and NGF variants that are useful in the treatment of multiple neurological diseases via the mechanism of promoting neurite outgrowth, see in particular columns 6-7 and 16-18. Mobley et al., further teach that a suitable assay to screen for such molecules is via assessing the ability of a molecule to

promote neuronal outgrowth in cultured dorsal root ganglia cultures, see Bioassay with dorsal root ganglia neurons, columns 19-20.

Mattson et al., teach protection of CNS neurons in culture from neuronal damage and death in a stroke model via treatment with nerve growth factor including after surgery or operation.

Olson et al., 1993 and Olson et al., 1994 teach the similarity in protection via nerve growth factor administration amongst different CNS model systems and predict its general applicability not only in the neurodegenerative diseases but for treatment of ischemia, stroke and injury, including treatment after surgery or operation, see in particular abstract.

Thus, Mobley et al., and Varon et al., Mattson et al., Olson et al., 1993 and Olson et al., 1994 teach the recognition in the art of neurotrophic factors to promote axon outgrowth in the CNS for a wide variety of diseases via mechanical introduction in patients, including for the stimulation of regeneration in treatments following surgery or operation. Mobley et al., further evidences that a suitable assay for predicting such effects is the dorsal root ganglia assay that was originally used in the characterization of NGF and now a multitude of known neurotrophic factors that are effective both in vitro and in vivo to promote neurite outgrowth within the PNS and the CNS in patients. Thus, one of skill in the art would have been motivated based on Kamata and Johnson's teachings of C3 exoenzyme as a neurotrophic factor capable of stimulating CNS neuronal outgrowth in dorsal root ganglia cultures to use the same molecule to produces such effects in vivo in a patient in need of CNS axon outgrowth, including

following operation or surgery as in spinal cord damage or transaction models. One of skill in the art would have expected success using such a method based on C3 exoenzyme's activity in promoting CNS axon outgrowth from DRG neurons in vitro and the art's teachings of such assays in predicting utility in promoting neurite outgrowth in the CNS of patients and the known art accepted models for establishing regeneration of axon outgrowth following surgery or operation as in regenerative models following spinal cord lesion. Thus, the cumulative reference teachings render the invention obvious to the skilled artisan. Applicant's comments with respect to the priority determination are particularly noted as it has been their position that the in vitro findings within the priority document combined with the prior art are sufficient basis for the artisan to be motivated to provide and expect success in in vivo treatments for the promotion of CNS neurite regeneration.

Status of Claims

11. No claims are allowed.

Conclusion

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.

Sharon L. Turner, Ph.D.
May 31, 2005
Primary Examiner 5-31-05